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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/214,723	01/11/1999	TAKANORI OKA	171-613P	8292

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EXAMINER
SISSON, BRADLEY L

ART UNIT	PAPER NUMBER
1634	21

DATE MAILED: 04/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/214,723	OKA, TAKANORI	
	Examiner	Art Unit	
	Bradley L. Sisson	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-10,12 and 13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-10,12 and 13* is/are rejected.

7)☒ Claim(s) *6 and 7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Location of Application

1. The location of the subject application has changed. The subject application is now located in Group 1630, Art Unit 1634.

Claim Objections

2. Claims 6 and 7 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 9 and 10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 9 and 10 are drawn to product, not method, wherein said product is a kit that comprises nucleic acid sequences. The claims do not define the chemicals in terms of what they are but rather, in terms of how they are to function. A review of the disclosure fails to find an adequate

written description of the broad genus of such chemicals. As set forth in *Enzo Biochem, Inc. v. Gen-Probe Inc.* (CAFC 01-1230 April 2002):

> [A]n adequate written description of genetic material "'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining he claimed chemical invention." Eli Lilly, 119 F.3d at 1566, 43 USPQ2d at 1404 (quoting *Fiers*, 984 F.2d at 1171, 25 USPQ2d at 1606). The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. Id. at 1568, 43 USPQ2d at 1406. A description of what the genetic material does, rather than what it is, does not suffice. Id.
> ***
> [H]ybridization from one DNA segment to another is just as much a functional definition as translation from a nucleic acid to a protein. As stated above, a description of genetic material by what it does - such as hybridizing to N. gonorrhoeae - is insufficient to satisfy § 112, ¶ 1, regardless whether the described property is labeled "chemical" or "functional."
> ***
> We also disagree with Enzo that binding affinity meets the test of an adequate description under the Guidelines.
> ***
> Describing a complicated molecule by means of a broad generic term (a nucleotide sequence) plus its function fails to distinguish it from other molecules that can perform the same function. A description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) having the function of lessening inflammation of tissues, fails to distinguish any steroid from others having the same activity or function. Similarly, the expression "an antibiotic penicillin" fails to distinguish a particular penicillin molecule from others possessing the same activity. Thus, in the absence of sequence information for its hybridization site, a nucleic acid described only by its ability to hybridize with another DNA fails to meet the requirement of § 112, ¶ 1.
> ***
> Application of the written description requirement, however, is not subsumed by the "possession" inquiry. A showing of "possession" is secondary to the statutory mandate that "[t]he specification shall contain a written description of the invention," and that requirement is not met if, despite a showing of possession, the specification does not adequately describe the claimed invention.

For the above reasons, and in the absence of convincing evidence to the contrary, the clams drawn to the chemicals per se have not been found to be adequately supported

by a written description in the specification and as such, are rejected under 35 USC § 112, first paragraph.

5. Claims 2-10, 12 and 13 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *In re Wands*, 8 USPQ2d 1400 (CAFC 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Quantity of Experimentation Necessary

The quantity of experimentation need is great, on the order of several man-years and then with little, if any, reasonable expectation of success.

The Amount of Direction or Guidance Provided and The Presence or Absence of Working Examples

The amount of guidance provided is quite limited. As seen in the examples (Example 1, page 25, lines 13-14; Example 2, page 28, lines 13-23; Example 4, page 33, lines 2-12; Example 5, page 36, lines 2-18), the non-labeled DNA, when present, was present at an amount of no less than 1%. The claimed method, however, places no limitation on the detection limit. As presently worded, the detection limit is seemingly

equal to whatever the fractional equivalent of the percentage of target DNA content in the sample; both are equated with the value "A/B." Given such a phenomenal relationship, the method seemingly encompasses the detection of an infinitely minute quantity of analyte nucleic acid.

The claims method calls for the identification and/or quantification of any mutation or polymorphism in a double standard sample DNA. It is noted that the method further requires the use of a labeled standard DNA that is to hybridize to the amplified analyte nucleic acid. In accordance with the recited method steps (claim 13), there is no separation of the admittedly labeled standard DNA from the duplex structure formed between the amplified target. Indeed, there is no method step recited which would allow for any differentiation between a hybridized target sequence from that of the complementary strand of the standard, which, as noted above, is required to be labeled. With the signal undoubtedly being the same whether there was any competitive hybridization or not, the signal will still be the same and one cannot detect, much less quantitate any of said mutations of polymorphisms that are present in the analyte nucleic acid.

In accordance with claim 7, the standard DNA is to now be amplified, yet there is no standardization of same. In view of such a predicament, the skilled artisan will be wholly unable to quantitate the results. Assuming that the amplified standard is still labeled, as is required in independent claim 13, all one is generating is more labeled standard. The method does not set forth, nor does the specification enable, a reproducible method whereby an unlimited supply of standard will result in the detection and quantification of any minute, or significant, quantity of analyte sequence.

While the level of skill in the art is high, on par with those that hold a Ph.D. in biochemistry, the five examples provided in the specification fail to address these issues in sufficient detail. It appears that applicant is relying upon the public to determine the types of starting materials applicable to the claimed method, as well as the reaction conditions under which the claimed method is to be practiced. Such shifting of the burden of enablement where as here it results in undue experimentation is in contrast with the statutory requirement of applicant providing a disclosure "in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same." See *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001.

The subject specification is effectively silent as to how these problems are to be overcome with respect to any level of detection.

Applicant is reminded that while the claims are read in light of the specification, limitations found therein are not read into the claims. But rather, the claims are read as broadly as is reasonably possible.

The Nature of the Invention

The claimed invention relates directly to matters of physiology and chemistry, which are inherently unpredictable and as such, require greater levels of enablement. As noted in *In re Fisher* 166 USPQ 18 (CCPA, 1970):

> In cases involving predictable factors, such as that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.

The State of the Prior Art

The aspect of competitive hybridization and mutation detection is known in the art. However, the art is not developed so as to permit the detection of any minute quantity of a target DNA, nor is the art developed to the point that non-specific conditions can be employed so as to detect a point mutation and/or quantitate same.

The Relative Skill of Those in the Art

The relative skill of those in the art that is most closely associated with the claimed invention is high, on par with those that hold a Ph.D. in biochemistry.

The Breadth of Scope of the Claims

The claims have sufficient breadth of scope so to encompass the detection of any minute quantity of a target DNA sequence with or without an amplified standard nucleic acid to which it is to hybridize. And as indicated above, the claims also encompass performing the claimed method without any separation or discrimination of duplex standard and duplex target-standard. In light of there not being any separation and without there being distinguishing characteristics between the analyte and the standard, and with there being no reduction in the amount of label present, the skilled artisan would

not be able to detect if any mutation(s) was present, much less quantify the amount of such a sequence of interest.

6. In view of the limited guidance provided and the art-recognized issues confronting such an assay, the specification has not been found to enable the claimed invention. Accordingly, claims 1-10, 12 and 13 remain rejected under 35 USC 112, first paragraph.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 2-8, 12 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claims 12 and 13 recite the limitation "the target DNA" in line 17 (claim 13) and line 2 (claim 12). There is insufficient antecedent basis for this limitation in the claim. It is noted that there is support for --the polymorphic target DNA."

Claims 2-10 which depend therefrom, fail to overcome this issue and are similarly rejected.

10. Claim 13, and claims 2-8 which depend therefrom, are confusing with respect to how the "analyte nucleic acid" relates to the "polymorphic target DNA."

11. Claim 8 recites the limitation "is the one prepared by chemical synthesis" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim.

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Conclusion

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is 703-308-3978. The examiner can normally be reached on Monday through Thursday from 6:30 AM to 5 PM.

13. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on 703-308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

14. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

B. L. Sisson

Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
April 11, 2002